Hyperparathyroid Bone Disease

Hyperparathyroid bone disease, also called *osteitis fibrosa cystica* (OFC), results from chronically elevated concentrations of parathyroid hormone (PTH). Elevated PTH concentrations may result from primary hyperparathyroidism, in which elevated PTH levels most often result from a parathyroid adenoma or rarely from hyperplasia or carcinoma.

Secondary hyperparathyroidism is an appropriate increase in PTH levels caused by malabsorption, vitamin D deficiency, or chronic renal failure. Calcium levels are normal or subnormal.

Tertiary hyperparathyroidism refers to elevated PTH resulting from long-standing stimulation of the parathyroid glands along with hypercalcemia, as in the setting of renal failure (see Chapter 73). Chronic stimulation results in hyperplasia or adenomas.

Primary and tertiary forms of hyperparathyroidism are characterized by hypercalcemia. Patients with secondary hyperparathyroidism are eucalcemic or hypocalcemic and have elevated PTH levels.

The skeletal disease in hyperparathyroidism is typified by *high turnover,* which is characterized by coupled increases in osteoclastic bone resorption and osteoblastic synthesis of osteoid, accelerated rates of bone mineralization accompanied by microcysts in the cortex and trabeculae (the *cystica* of OFC), and increased numbers of fibroblasts and marrow stroma (the *fibrosa* of OFC) (see Fig. 74-1B and D). Levels of both serum markers of bone formation (i.e., alkaline phosphatase and osteocalcin) and markers of bone resorption (i.e., N-terminal and C-terminal telopeptides) are usually increased, reflecting the bone histology. Patients may complain of bone pain or diffuse aches and pains.

Bone density, assessed by dual-energy x-ray absorptiometry (DEXA), may be normal or low. The pathognomonic radiologic signs of severe hyperparathyroid bone disease are a salt-and-pepper appearance of the calvarium, resorption of the tufts of the terminal phalanges and distal clavicles, subperiosteal resorption of the radial aspect of the cortex of the second phalanges (Fig 74-3), and Brown tumors (i.e., collections of osteoclasts that produce gross lytic lesions) of the pelvis and long bones. These radiologic signs disappear with parathyroidectomy, and bone mass, as assessed by DEXA, typically increases rapidly and markedly after parathyroidectomy.

The treatment of hyperparathyroid bone disease involves remediation of the chronically elevated PTH concentrations by parathyroidectomy in primary or tertiary hyperparathyroidism or correction of the underlying cause of secondary hyperparathyroidism (see Chapter 73). If the hypercalcemia is mild and the bone mass is normal, no treatment may be required.

Serum calcium levels can be reduced by using a parathyroid calcium receptor mimetic. Cinacalcet is indicated for patients with chronic renal failure with secondary hyperparathyroidism, patients with parathyroid carcinoma who have failed surgical resection, and patients with severe primary hyperparathyroidism.

Moderate to severe hypocalcemia may be seen after parathyroidectomy. This condition is referred to as the *hungry bone syndrome* (see Chapter 73). Hyperparathyroid bone disease may be *pure,* occurring in patients with severe primary

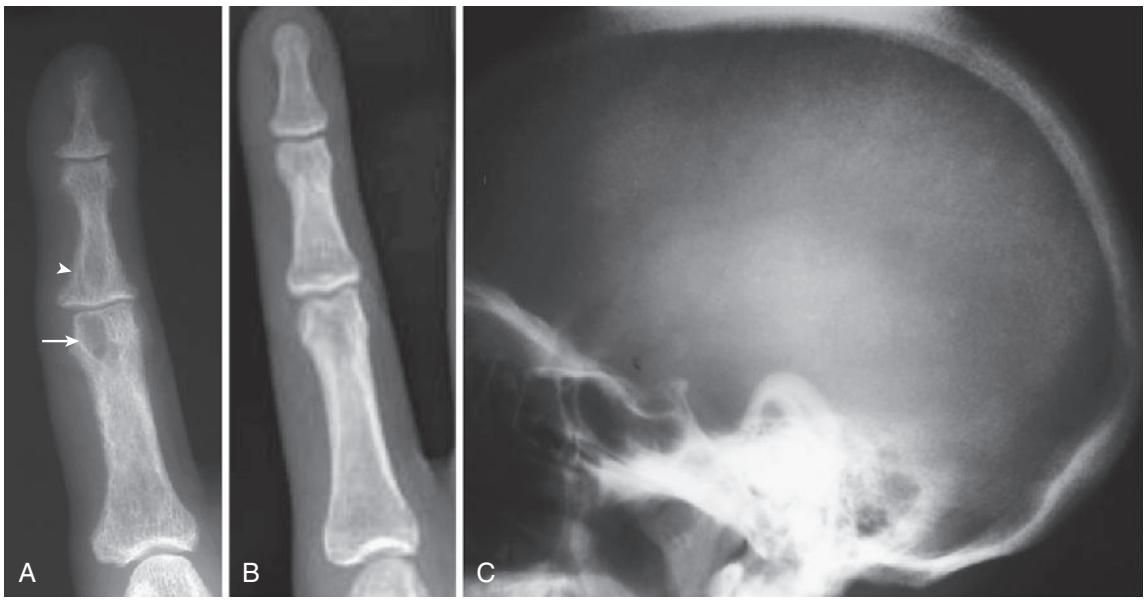

FIGURE 74-3 Skeletal radiographic changes of hyperparathyroidism. **A,** A hand film from a patient with primary hyperparathyroidism. The *arrow* indicates a typical giant cell tumor (brown tumor), which is a collection of osteoclasts that lead to macrocystic changes in bone. The *arrowhead* indicates the irregular radial surface of a phalanx resulting from subperiosteal bone resorption, which is typical of hyperparathyroidism. The brown tumor and the subperiosteal resorption refill and disappear when the offending parathyroid tumor or hyperplasia is resected. **B,** Radiograph of a normal hand for comparison. No brown tumors are seen, and the phalangeal periosteal surfaces are smooth. **C,** The classic salt-and-pepper appearance of the skull in hyperparathyroidism. The periosteal surfaces of the inner and outer cortices or tables of the calvarium are indistinct as a result of subperiosteal bone resorption. The lateral view of the calvarium is hazy and indistinct, showing micropunctations. (Courtesy J. Towers, MD, and D. Armfield, MD, University of Pittsburgh, Pittsburgh, Penn.)